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Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(54) Title: STEALTHY POLYMERIC BIODEGRADABLE NANOSPHERES AND USES THEREOF

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(57) Abstract: Disclosed herein are stealthy polymeric biodegradable nanospheres each comprising: (i) a polyester-polyethylene multiblock copolymer; (ii) optionally a polyester entangled with the multiblock copolymer to give rigidity to the nanospheres; and (iii) optionally a pharmaceutical compound incorporated therein. Also disclosed is the use of such nanospheres for the preparation of a medicament having a long-term and non-toxic release of a pharmaceutical compound into a mammal, and the method for preparing a stealthy polymeric biodegradable nanospheres.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/CA 03/00499

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K9/51

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EP0-Internal, WPI Data, PAJ, EMBASE, BIOSIS, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 139 870 A (VERRECCHIA THIERRY) 31 October 2000 (2000-10-31) the whole document -----	1-3, 13-17, 19-21, 37-39
X	US 5 683 723 A (BAZILE DIDIER ET AL) 4 November 1997 (1997-11-04) the whole document ----- -/-	1-3, 13-21, 37-39, 41

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the International filing date but later than the priority date claimed

"T" later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the International search

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16 MAR 2004

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/CA 03/00499

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01/012718 A (SEO MIN HYO ;CHOI IN JA (KR); SAMYANG CORP (KR)) 22 February 2001 (2001-02-22) page 4, paragraph 4 - page 5, paragraph 1 page 5, last paragraph - page 6, paragraph 3 page 8, paragraph 2 page 10, paragraph 2; claims 1,3,6,19,12,15,16,18; examples 10,11 -----	1-3, 13-17, 20,21, 37,39
X	NAKADA Y ET AL: "LONG-CIRCULATING NANOPARTICLES USING BIODEGRADABLE ABA TRIBLOCK COPOLYMERS CONTAINING POLY(L-LACTIC ACID) A-BLOCKS ATTACHED TO CENTRAL POLY(OXYETHYLENE) B-BLOCKS" PHARMACEUTICAL SCIENCES, LONDON, GB, vol. 3, no. 10, October 1997 (1997-10), pages 479-481, XP000783648 ISSN: 1356-6881 the whole document -----	1-3, 13-21, 37-39,41
X	RYU JAE-GON ET AL: "Clonazepam release from core-shell type nanoparticles of poly(epsilon-caprolactone)/poly(ethylene glycol)/poly(epsilon-caprolactone) triblock copolymers" INTERNATIONAL JOURNAL OF PHARMACEUTICS (KIDLINGTON), vol. 200, no. 2, 10 May 2000 (2000-05-10), pages 231-242, XP002257858 ISSN: 0378-5173 page 232, right-hand column, paragraph 3 - page 233, left-hand column, paragraph 2 page 235, left-hand column, last paragraph - right-hand column, paragraph 1 -----	1-3,13, 15-17, 20,21, 37-39
X	PANOYAN AVEDIS, HILDGEN PATRICE: "Vecteurs polymériques injectables pour l'administration des anticancéreux" CONGRÈS DE L'ACFAS 2000 - COMMUNICATION PRÉSENTÉE AU CONGRÈS, [Online] page 1, XP002257860 Retrieved from the Internet: <URL: http://www.acfas.ca/congres/congres68/S1080.htm> [retrieved on 2003-10-14] Last modified: 20-3-2002 the whole document -----	1-3, 13-21, 37-39

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/CA 03/00499

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 007 845 A (GREF RUXANDRA ET AL) 28 December 1999 (1999-12-28) column 3, line 66 - column 4, line 22 column 6, line 63 - column 7, line 11 column 9, line 19 - line 39 column 12, line 65 - column 13, line 4 claims 6,8,10,11,13,14,20,24,26,28,29; example 20 -----	1,3, 13-15, 17-21, 37,39,40

INTERNATIONAL SEARCH REPORT

International Application No.
PCT/CA 03/00499

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 21 and 37-40 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the composition.
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-21;37-40;41-44 partially

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-21; 37-40,41-44 partially

A stealthy polymeric biodegradable nanosphere comprising a polyester-polyethylene multiblock copolymer, use thereof for the preparation of a medicament, a method for delivering a pharmaceutical compound into a mammal by administration thereof, and method for preparation thereof.

2. claims: 22-28

A polyester-polyethylene multiblock copolymer of formula (III): $ABA-B'-(ABA-B')n-ABA$ (III), wherein A is a polyester, B is a polyethylene, B' is a dicarboxylic polyethylene and $n \geq 2$. And a method for preparing the polyester-polyethylene multiblock copolymer of formula III.

3. claims: 29-36

An improved method for preparing a PLA-PEG-PLA multiblock copolymer of formula (I): $ABA-(c-ABA)n-c-ABA$ (I), wherein ABA is a PLA-PEG-PLA triblock, c is a carboxylic diacid, and $n \geq 2$.

4. claims: 41-44 partially

Method for preparing a stealthy polymeric biodegradable nanospheres from an emulsion, comprising the steps of (i) preparing an organic internal phase comprising a pharmaceutical compound and a blend of polymers and a polyester; (ii) preparing an aqueous external phase; (iii) injecting both phases into a homogenization chamber having an outlet; (iv) evaporating and/or extracting the phases of step (iii); collecting the stealthy polymeric nanospheres by centrifugation or dialysis.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/CA 03/00499

Patent document cited in search report	Publication date		Patent family member(s)	Publication date
US 6139870	A 31-10-2000		FR 2742357 A1 AU 1180097 A EP 0869776 A1 WO 9722337 A1 JP 20000501989 T ZA 9610601 A	20-06-1997 14-07-1997 14-10-1998 26-06-1997 22-02-2000 24-06-1997
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